WHAT IS CLAIMED IS:

1. A method for enhancing identification and relative quantitation of proteins and peptides using mass spectrometry (MS), said method comprising the steps of:

(a) reducing the disulfide bonds of a first sample from a biological mixture containing proteins and peptides;

(b) labeling proteins and peptides in the first sample with a reagent which comprises a thiol-specific reactive group attached to a guanadino group via a linker which can be differentially labeled;

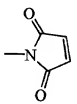
(c) separating the proteins and peptides from the sample;

(d) digesting the proteins to provide a mixture containing digestion peptides and peptides from the first sample; and

(e) subjecting the peptides of (d) to quantitative MS analysis and protein identification.

2. The method according to claim 1, wherein the peptides of (d) are subjected to matrix-assisted laser desorption/ionization (MALDI) - MS.

3. The method according to claim 1, wherein the reagent comprises a thiol-specific reactive group is selected from the group consisting of α-haloacetyl (-X-CH_2CO-, X = I, Br, or Cl) or a maleimide group having a structure selected from the group consisting of:



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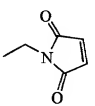


4. The method according to claim 1, wherein the linker comprises an alkyl chain having three to eight carbon atoms, optionally substituted with one or more amido groups, carboxy groups, or amino groups.

5. The method according to claim 1, wherein the proteins and peptides are further subjected to peptide mass mapping, said method further comprising the steps of:

labeling proteins and peptides in a second sample with said reagent having heavy stable isotopes; and

mixing the first and second samples prior to the separation step,

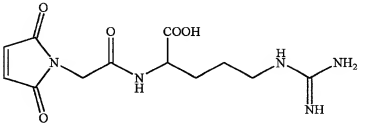
wherein the reagent in the labeling step contains light stable isotopes.

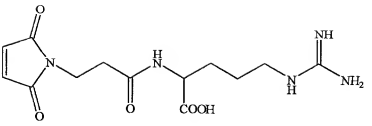
6. The method according to claim 1, wherein the linker in the reagent of step (b) contains a substitution of four to twelve atoms with a stable isotope.

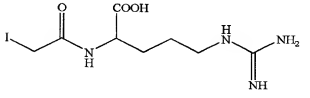
7. The method according to claim 6, wherein the linker contains seven stable isotopes.

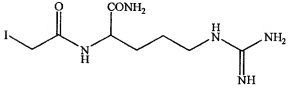
8. The method according to claim 6, wherein the hydrogen atoms are substituted with deuterium.

9. The method according to claim 5, wherein the reagent is selected from the group consisting of:









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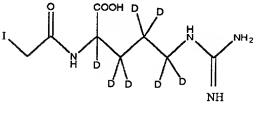


10. The method according to claim 5, wherein the separation step is performed using one dimensional or two dimensional polyacrylamide gel electrophoresis (1D or 2D-PAGE), or liquid chromatography.

11. The method according to claim 1, wherein the digestion step is performed in-gel or in solution.

12. A method for preparing peptides for MALDI-MS and subsequent data analysis, said method comprising the steps of:

(a) reducing the disulfide bonds of proteins from biological samples;

(b) labeling proteins in one sample with a reagent which comprises a thiol-specific reactive group attached to a guanidino group via a linker which is differentially labeled with light stable isotopes;

(c) labeling proteins in a second sample with a reagent having heavy stable isotopes;

(d) mixing the first and second labeled samples;

(e) separating the proteins from the mixture;

(f) digesting the proteins, thereby providing peptides ready for MALDI-MS analysis and protein identification.

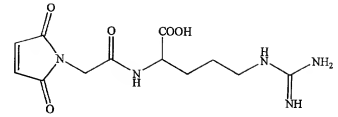
13. The method according to claim 11, wherein the digestion step is performed using trypsin.

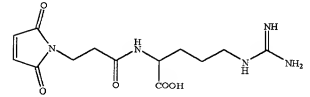
14. A compound useful in quantitative analysis of protein mixtures, said compound comprising a thiol-specific reactive group attached to a guanidino group via a linker which can be differentially labeled with stable isotopes.

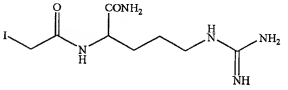
15. The compound according to claim 14, wherein the linker contains four to twelve stable isotopes.

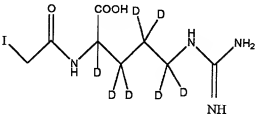
16. The compound according to claim 14, wherein the linker contains a substitution of at least six hydrogen atoms with deuterium.

17. The compound according to claim 14, selected from the group consisting of:









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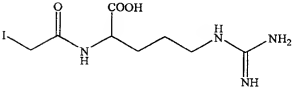

18. A reagent kit for the analysis of proteins by mass spectrometric analysis that comprises a compound of claim 14 or claim 17.

19. The reagent kit according to claim 18, comprising a set of substantially identical differentially labeled alkylating reagents.

20. The reagent kit according to claim 18, further comprising one or more proteolytic enzymes for use in digestion of proteins modified by said compounds.